Retrovirus Epidemiology Donor Study-II - Coordinating Center
RFP: NHLBI-HB-04-16

DESCRIPTIONS AND STATEMENT OF WORK FOR SOLICITATION PURPOSES

a. General Description of the Required Objectives and Desired Results

The objectives of the REDS-II Study are to conduct epidemiological, laboratory, and survey research on volunteer blood donors within the United States to ensure the safety and availability of the United States' blood supply. This includes monitoring known blood-borne infectious agents, rapidly evaluating the impact of emerging pathogens, assessing the safety implications of changes in laboratory and/or blood donor screening protocols and examining blood supply and availability issues. Addressing issues concerned with the safety and availability of the United States' blood supply will be the cornerstone of the Institute's REDS program. These issues include: a) the risks of transfusion-transmissible infections and their trends through time - these include infectious agents currently undergoing laboratory screening as well as new and emerging agents such as West Nile Virus (WNV) which is about to be screened for in the U.S. under experimental protocols; b) ways to reduce the risks of transfusion-transmissible infections; c) HIV, HTLV, HCV, and HBV test screening methodologies; d) donor characteristics, behaviors, and donation return patterns of U.S. blood donors; and e) the effectiveness and safety of various strategies implemented to increase the U.S. blood supply.

b. Background Information

REDS was established to address important blood safety issues involving human retroviruses. An RFP was released in 1988 soliciting proposals to study the epidemiology of human retroviruses in volunteer blood donors. On July 17, 1989 the NHLBI awarded contracts to five major blood centers and a coordinating center to develop a major multi-center epidemiologic study of the human retroviruses HIV-1, HIV-2, HTLV-I, and HTLV-II in volunteer U.S. blood donors. During the first year, the Steering Committee developed the study protocol, manual of operations and the data collection forms to provide a framework for the rapid response to research questions of critical importance to the safety of the blood supply, particularly with regard to issues related to retroviruses and other transfusion-transmitted agents. In 1994, a second group of contracts was awarded by NHLBI to the five blood centers and coordinating center and in 1999, a third group of contracts was awarded to the five blood centers and coordinating center. The 1989 awards were made as a result of a full and open competition. The 1994 and 1999 awards were made using the JOFOC mechanism.

The original mission of REDS was to initiate and facilitate investigations of human retroviruses in volunteer blood donors from areas of the United States at varying risk for HIV. During the course of the project, NHLBI expanded the original REDS mission to investigate critical questions posed by the blood banking and transfusion medicine communities that were essential to ensuring an adequate blood supply without compromising blood safety. The overall REDS program includes epidemiologic, laboratory, and clinical investigations, and provides a comprehensive framework for monitoring U.S. blood donations, and more recently transfusion recipients, for infectious disease markers. The operational and database structure of REDS, specifically designed to study blood safety and availability in the United States, has also provided a framework for rapid analytical response to other research questions of significant importance to the safety of the blood supply.

REDS currently consists of five U.S. blood centers and a coordinating center. Since its inception, REDS investigators have made major contributions in assessing: the risk of contracting transfusion-transmitted infectious agents; HIV and HCV test screening; donor characteristics and behaviors; and ways of reducing HIV risk from transfusion. REDS investigators work closely with the FDA, CDC and Office of the Secretary, DHHS to provide data and analyses for important policy decisions. Liaisons with test manufacturers have enabled the rapid study of test procedures of critical importance to blood safety and availability.

Data Monitoring - The five REDS blood centers have compiled over 12.6 million donation records from more than 3.7 million U.S. blood donors through 2002. This database has permitted REDS investigators to estimate incidence, prevalence and risk of transfusion-transmitted agents, and provides the sampling frames for laboratory and epidemiology studies.

Repositories - Two repositories of more than 600,000 serum specimens representative of the U.S. donor population with demographic and test result information have been established. Smaller special repositories have also been established. REDS investigators created a matched donor-recipient repository containing blood samples from U.S. blood donors and from recipients of these donors' blood. This repository, the Retrovirus Allogeneic Donor and Recipient Repository (RADAR), will be made available for use to the scientific community for scientifically meritorious studies and will enable investigators to determine the prevalence and transfusion transmissibility of newly identified and emerging infectious agents.

Laboratory Studies - REDS has conducted numerous laboratory studies documenting the accuracy of HIV screening and confirmatory assays and quantifying the beneficial and potential adverse impacts of new screening measures. Other studies include a comparison of the sensitivity and specificity of HIV and HCV viral nucleic acid screening assays used to screen the nation's blood supply and development of protocols to evaluate a West Nile Virus RNA screening assay(s).

Epidemiology Studies - REDS has conducted surveys to estimate the prevalence of unreported risk behaviors in the U.S. blood donor population and to evaluate the prevalence and impact of donation incentives. To address the critical problem of blood shortages facing the nation today, REDS is conducting a survey study to assess donor motivation and to examine why donors do not donate more frequently. Issues regarding donation experience, accessibility to donate, and the influence of altruism as an impetus to donate will be evaluated. The REDS donation database will be used to assess stated intent versus actual donation behavior.

c. Detailed Description of the Technical Requirements

The goal of this multicenter epidemiologic study is to address scientific questions to improve the safety and adequacy of the U.S. blood supply. Objectives of the study are to: 1) Assess the prevalence and incidence of existing as well as newly discovered infectious agents that pose a threat to blood safety; 2) evaluate characteristics and behaviors of blood donors; 3) assess the impact of existing and new blood donor screening methodologies; 4) assess the impact of new blood bank technologies on blood safety and availability; and 5) evaluate the donation process for ways to improve the adequacy of the blood supply.

The study will include survey and epidemiological research as well as laboratory investigations. Comprehensive donor and donation databases will enable study investigators to provide the scientific and analytical expertise needed to address important blood safety issues and to respond in a timely manner to scientific and policy concerns and to "crises" that threaten the blood supply. It

is anticipated that six to eight blood center awards, one central laboratory award, and one coordinating center award will be made.

The Coordinating Center will be expected to collect monthly U.S. blood donation data from 6-8 participating blood centers representing a minimum of between 170,000 and 220,000 donations annually from an estimated 120,000 to 160,000 donors. During the course of the study, the Coordinating Center will be expected to process survey forms for one or two major studies with an estimated 15,000 - 50,000 U.S. blood donor subjects each. The mode of survey administration will depend upon the study design. It is expected that the laboratory component of the study will generate about 4 studies annually for which the Coordinating Center will process, manage, and analyze data.

The Study will be performed in the following phases:

Phase 1	9 months	Development of study protocols, design of forms, and manual of operations
Phase 2	45 months	Study enrollment, conduct of surveys, laboratory testing
Phase 3	6 months	Data analysis and preparation of publications

ARTICLE C.1. STATEMENT OF WORK

a. Independently and not as an agent of Government, the contractor shall furnish all the necessary services, qualified personnel, material, equipment, and facilities, not otherwise provided by the Government as needed to perform the Statement of Work below. The contractor shall deliver the items specified in ARTICLE F.1. to the destinations indicated.

The Coordinating Center will be expected to collect monthly U.S. blood donation data from 6-8 participating blood centers representing a minimum of between 170,000 and 220,000 donations annually from an estimated 120,000 to 160,000 donors. During the course of the study, the Coordinating Center will be expected to process survey forms for one or two major studies with an estimated 15,000 - 50,000 U.S. blood donor subjects each. The mode of survey administration will depend upon the study design. It is expected that the laboratory component of the study will generate about 4 studies annually for which the Coordinating Center will process, manage, and analyze data.

Specifically, the Contractor shall serve as the coordinating center for the Retrovirus Epidemiology Donor Study-II (REDS-II) and shall perform the following study requirements:

1. Coordinate and participate in development and finalization of study protocols and design of study forms. Reproduce and distribute Study protocols and forms. Study protocols shall be reviewed by the Observational Study Monitoring Board and must be approved in writing by the Project Officer.

2. Coordinate and participate in the development of a manual of operations which describes in detail proper procedures for data collection. Donation data delivery requirements should include detailed guidance on the contents of the files to be delivered, as well as the mode and time line for data delivery. Guidance on the demographic and laboratory testing data fields and the field requirements, including acceptable codes and field sizes, must be included in the manual of operations. The manual of operations for surveys will include specific instructions on how to administer and collect the survey data specific to the type of survey being conducted (in-person, web, or direct mail). The Contractor shall assume responsibility for the reproduction

and distribution of the manual of operations including updates. **The Draft Protocol entitled: Retrovirus Epidemiology Donor Study-II (REDS-II), dated June 2003 (Exhibit 1) is hereby made part of the contract. It is mutually agreed that future revisions of this Protocol and the Manual of Operations are considered to be incorporated by reference into this contract without further contract modification.**

3. Arrange for Steering Committee meetings and other key meetings as needed and take and distribute minutes of the meetings. The Principal Investigator for the coordinating center shall attend Steering Committee meetings and be a member of the Committee.

4. Arrange for Observational Study Monitoring Board meetings and prepare reports as necessary.

5. Develop and implement data collection procedures for the epidemiologic and survey studies. Perform all activities of a coordinating center such as collecting, organizing and storing for analysis data from blood centers including infectious disease marker data (screening and confirmatory data) and donor demographic data (age, race, gender, education, ethnicity, country of birth, history of transfusion) and study data from the central laboratory. Assure the quality of the study data submitted and stored. Provide support and documentation for the OMB forms clearance process if necessary.

6. Train the staff at blood centers in entry of data and completion of study forms.

7. Have primary responsibility to assure prompt accumulation, entry, and editing of study data (screening, baseline, periodic follow-up, special events). Assume data will be collected from a minimum of between 120,000 and 160,000 U.S. blood donors per year.

8. Communicate with the blood centers and central laboratory concerning missing, delayed, incomplete, or erroneous data.

9. Obtain and process laboratory test reports from the study's central laboratory as required by protocol. Coordinate compilation of data collected by the study's central laboratory into a study database for subsequent statistical analysis. Perform quality control checks and editing of data generated by the laboratory. Maintain a record of the studies conducted, the number and types of samples used, and the results of analyses conducted by the central laboratory. Compile and manage an inventory of specimens (e.g., serum, plasma, blood, etc.) shipped to and received by the central laboratory form the blood centers.

10. Prepare quarterly and annual technical progress reports and others as needed to monitor study progress, quality of data and blood center performance, (participant enrollment and compliance, and form completion, response variables, and adverse reactions).

11. Interact with the Project Officer on issues relating to study design, study conduct, and data analysis.

b. Reference Material

Exhibit 1 - Draft Protocol entitled: Retrovirus Epidemiology Donor Study-II (REDS-II), dated June 2003, 9 pages.

c. Clinical Research/Human Subjects

REDS-II will study United States blood donors. The youngest legal age for blood donation is seventeen, so donors between the ages of seventeen and twenty-one will be considered children. Human subject assurance certification by contractor's IRB must be obtained prior to participant contact. Applicable clauses will be incorporated into any resultant contract. The following guidelines and policies, which may be applicable to this solicitation, can be viewed at: http://www.nhlbi.nih.gov/funding/policies/index.htm and will be incorporated into the resultant RFP.

- NHLBI Guidelines for Implementation of the Policy on Inclusion of Minorities and Women in Study Populations
- NHLBI Guidelines for Implementation of the Policy on Inclusion of Children in Research Involving Human Subjects
- Terms and Conditions for Accrual of Research Subjects in Research Supported by NHLBI
- Establishing Observational Study Monitoring Boards
- Responsibilities of OSMBs Appointed by the NHLBI
- Guidelines for Data Quality Assurance in Clinical Trials and Observational Studies
- Avoiding Conflicts of Interest in Multi-Center Clinical Trials—Guidelines
- Human Tissue Repositories—Guidelines
- Tissue Sharing in Informed Consent—Guidance

d. Special Requirements

1. OMB Clearance

   Once the REDS-II Protocol has been approved, a request for clinical exemption for REDS-II generated forms will be coordinated by the NHLBI Project Officer for submission to the NIH OMB Clearance Officer. It is expected that the forms used by REDS-II contractors to collect data will be exempt from OMB forms clearance requirements.

2. The Government does not plan to support alteration or renovation of space to complete the objectives of the contract. Thus, facilities and equipment necessary to complete the work proposed must be furnished by the offeror for use during the course of the contract. Furthermore, the procedures and facilities to obtain informed consent, to code the samples and to maintain confidentiality of test results must also be established and available at the start of the contract.

3. IRB Approval

   The contractor will be required to obtain IRB approval for CC activities described in the REDS-II Protocol and any amendments thereto.

e. Level of Effort

	Percent of Effort*		
	Phase 1	Phase 2	Phase 3
Principal Investigator	25%	25%	15%
Project Director	100%	100%	50%
Epidemiologist	50%	100%	50%
Biostatistician	25%	50%	20%
Statistical Programmer	10%	40%	10%

Programmer	0%	50%	10%
Research Assistant	0%	50%	10%
Data Prep Supervisor	0%	30%	10%
Data Entry	0%	50%	10%
Secretarial	50%	100%	20%
Coder/Clerk	0%	40%	20%
	260%	635%	225%

- Phase 1 - Planning is 9 months;
- Phase 2 - Study enrollment, conduct of surveys, laboratory testing is 45 months; and
- Phase 3 - Data analysis and preparation of publications is 6 months.

Coordinating center staff or consultants must have transfusion medicine, blood banking, and infectious disease expertise.

Coordinating Center Staffing Requirements: Direct labor devoted to the project must be compatible with the scientific and technical approach described in the Draft Protocol and the activities included in the Statement of Work. Effort is shown as a percentage of FTE (full-time equivalent) labor. The personnel and levels of effort listed below are for information only and are not to be considered restrictive for proposal purposes. The levels were formulated by NHLBI staff experienced in the conduct of multicenter epidemiology studies. Personnel with experience relevant to the operation of a coordinating center for multicenter epidemiologic, survey, and laboratory studies in the area of blood banking and transfusion medicine are required.

Note: Offerors shall ensure that the PI and all other personnel proposed will not be committed on Federal grants and contracts for more than a total of 100% of their time. If the situation arises where it is determined that a proposed individual is committed for more than 100% of his or her time, the Government will require action on the part of the offeror to adjust the time commitment.

f. Travel

Travel costs should be based on attendance at the following meetings:

Steering Committee (3 CC attendees) three meetings during the nine-month protocol development phase (Phase 1) and two meetings per year thereafter (Phase 2). Meetings to be held in Bethesda, Maryland for two days each.

Observational Study Monitoring Board (2 CC members) to attend one meeting per year in Bethesda, Maryland. Proposed costs should include travel expenses for five members of the Observational Study Monitoring Board to attend a one-day meeting.

Site visits to Blood Centers (two CC participants). Assume three site visits per year.

g. Study Committees

Steering Committee: The chairperson of the Steering Committee will be appointed by the NHLBI. The steering committee will meet at designated intervals with the NHLBI project officer and other interested parties. The Steering Committee will be composed of Retrovirus Epidemiology Donor Study-II Principal Investigators and Study Coordinators from each Blood Center, principal

investigator and co-investigators of the Coordinating Center, principal investigator from the central laboratory, and NHLBI staff representatives. The Coordinating Center will be responsible for organizing and planning the meeting. Steering Committee members are expected to participate in writing committees and other subcommittees as needed. Decisions to develop and implement study protocols will be made and voted upon by Steering Committee members. There will be only one designated voting member per Blood Center, one from the central laboratory, and one from the coordinating center. A designated voting member (e.g., Principal Investigator or representative) must be present to vote. The Steering Committee will meet semi-annually in Bethesda, Maryland.

The **Publications Committee** will review and evaluate all proposed oral/poster presentations and manuscripts that will utilize study data. Recommendations of the Publications Committee will be forwarded to the NHLBI for review.

An **Observational Study Monitoring Board (OSMB)**, appointed by the NHLBI will review the protocol during the planning phase and thereafter periodically review the progress of the study, evaluate results, and make recommendations concerning the operation of the study. This committee will be comprised of experts in relevant biomedical fields, biostatistics, and bioethics who have no direct relationship with the study. Annually the Observational Study Monitoring Board (OSMB) will review summaries of data provided by the Coordinating Center. If any conclusions bearing on patient safety are made, they will be communicated to the blood center principal investigators and patients promptly. Data will be privileged and shared only with the Observational Study Monitoring Board during Phase II. The chairman of the Steering Committee, staff from the coordinating center, and staff from the Project and Contracts offices will attend meetings of the OSMB. The Board will meet once per year and conduct teleconferences as needed. Responsibilities of OSMBs appointed by the NHLBI can be found at: http://www.nhlbi.nih.gov/funding/policies/osmb_inst.htm

h. Proposals should include the following information:

1. Provide the names, degrees, training, qualifications, experience, role in project, and effort for each individual proposed.

2. Document the experience of the proposed personnel in the administration and management of multi-center epidemiology programs.

3. Propose detailed procedures for data collection and entry by the Blood Centers (BC), transmission of data to the Coordinating Center (CC), and storage by the CC.

4. Propose in detail methods for assessing and reporting the quality of data received from the Blood Centers and the Central Laboratory.

   Note: The Coordinating Center will be expected to collect monthly donation data from six to eight participating blood centers representing a minimum of between 170,000 and 220,000 donations annually from an estimated 120,000 to 160,000 donors. During the course of the study, the Coordinating Center will be expected to process survey forms for one or two major studies with an estimated 15,000 - 50,000 subjects each. The mode of survey administration will depend upon the study design. It is expected that the laboratory component of the study will generate about four studies annually for which the Coordinating Center will process, manage, and analyze data.

5. Describe computer systems and software to be employed by the Coordinating Center, Blood Centers, and Central Laboratory.

6. Describe materials and methods of instruction for training Blood Center and Laboratory personnel in procedures for data collection and management.

7. Propose methods for assuring the privacy of human research subjects.

8. Provide a detailed description of facilities that will be used to carry out the Statement of Work. Identify where computer systems will reside and which staff will have access.

   Note: According to the FAR and DHHS policy, contractors are expected to possess all the resources needed to perform a Government contract (including general purpose equipment.)

9. Describe the administrative structure of the CC.

10. Describe plans for arranging and coordinating meetings of the REDS committees and boards. Plans should include discussion of reimbursement for meeting rooms, travel, hotel, and per diem expenses. The CC will be responsible for the reimbursement of honorarium ($200/day) and travel expenses for the Observational Study Monitoring Board members for their participation and attendance at REDS-II meetings.

11. Describe any institutional commitments that will be provided if selected for award.

12. Provide documentation of an Office of Human Research Protections-approved institutional assurance (e.g. an FWA).

13. Provide any other information needed to allow reviewers to judge the capability of the offeror to accomplish the Statement of Work of the CC.